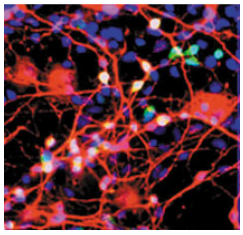
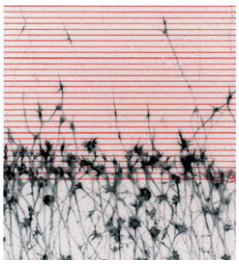


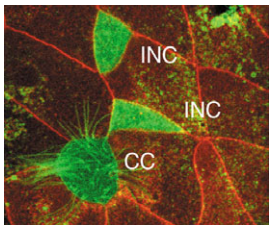
Hes1 sets boundaries

The developing central nervous system is divided into compartments (which later form distinct populations of neurons) by boundary cells. These slowly proliferating, non-neuronal cells control neuronal specification in neighbouring compartments, but what regulates boundary formation? Baek and colleagues now report that persistent high levels of the bHLH transcription factor Hes1 regulate the formation of five boundaries (the floor plate, isthmus, rhombomere, roof plate and zona limitans intrathalamica boundaries) in the developing mouse brain (see p. 2467). They show first that Hes1 expression in non-boundary cells is variable but is always high in boundary cells. Then, by manipulating the expression of Hes1 in both cell types in vivo and in vitro, the researchers demonstrate that persistent high levels of Hes1 expression repress the expression of proneural transcription factors and reduce cell proliferation rates. Conversely, the absence of *Hes1* (and also of *Hes3* and *Hes5*) disrupts the organizing centres of the developing nervous system, thus confirming the importance of Hes1 expression in boundary formation.



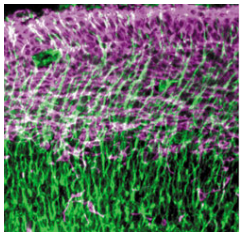
New technique for guiding axons

Axons navigate to their targets during brain development by interacting with gradients of guidance molecules. Exactly how they read these gradients is unclear. Now on p. 2487, Friedrich Bonhoeffer, Martin Bastmeyer and co-workers propose that chick retinal axons stop growing in response to the combined effect of the total amount of ephrin5A that they have encountered during their outgrowth and its local concentration. The researchers investigated the response of chick retinal growth cones to different gradients and local concentrations of ephrin5A by using a new technique – microcontact printing – to prepare reproducible and quantifiable, discontinuous gradients of this guidance molecule on coverslips. They found that the growth cones stopped at distinct zones within these gradients but remained active rather than collapsing. The position at which they stopped depended on both the steepness of the gradient and the local concentration of substrate-bound ephrin. Whether a similar mechanism acts in vivo – where growth cones are reading several gradients simultaneously – remains to be investigated.



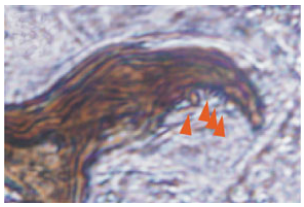
Skin deep cell patterns

The functioning of certain tissues and organs relies on a directed flow of fluid that is produced by epithelial cells that bear motile cilia. Stubbs et al. have been investigating how ciliated cells insert into one such tissue – the skin of *Xenopus* embryos – in an evenly spaced pattern (see p. 2507). Ciliated cell precursors (CCPs) are produced in the inner ectodermal layer before radially intercalating into the outer ectodermal layer. Notch signalling determines the number of CCPs, but when it is inhibited, the epidermal pattern of ciliated cells is mostly unchanged even though more CCPs are produced. The researchers use confocal microscopy to show that CCPs can 'wedge' anywhere between the outer ectodermal cells at their basal surfaces, but only insert apically and singly where at least three outer layer cells make contact. Thus, they suggest, the normal pattern of ciliated cells is maintained when CCPs are overproduced because access sites in the outer ectodermal layer are limited and only one CCP can fit into each site.



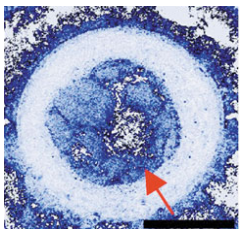
STAT acts via Notch to maintain neural precursors

The three major cell types of the mammalian central nervous system are all derived from neural precursor cells (NPCs). The undifferentiated state of NPCs is maintained by Notch signalling and secreted growth factors; NPCs divide a fixed number of times before differentiating to ensure that the brain contains the right mix of cells. Now, on p. 2553, Yoshimatsu and colleagues report that STAT3 (signal transducer and activator of transcription 3) acts in a non-cell-autonomous manner through the Notch ligand Delta-like 1 (DLL1) to maintain NPCs in the embryonic mouse neocortex. They show that NPCs express STAT3 and that deletion of *Stat3* in a subset of cells in vivo and in vitro produces premature neurogenesis in their neighbours. STAT3, they report, regulates the expression of DLL1. Moreover, the knockdown of DLL1 by RNAi blocks the ability of STAT3 to maintain NPCs. The authors suggest that this previously unrecognized interaction between STAT3 and Notch signalling might maintain other stem cell populations during development.



From Neverland: insights into steroid hormone synthesis

Steroid hormones coordinate many aspects of growth and development in metazoans. In insects, ecdysteroids, such as ecdysone, are made in the prothoracic gland (PG) and control moulting and metamorphosis, but little is known about the early steps of their biosynthesis from cholesterol. Niwa, Kataoka and co-workers now report that Neverland (Nvd) – a novel, conserved oxygenase-like protein – is required early in ecdysone synthesis and is essential for silkworm and *Drosophila* growth (see p. 2565). The researchers identified *nvd* by looking for genes predominantly expressed in the PG of silkworms. *nvd* is conserved in *Drosophila*, nematodes and several chordates (but not mammals), and the researchers show that loss of *nvd* function in the PG arrests growth and moulting in *Drosophila* larvae. This arrest can be rescued by the addition of active ecdysone or its precursor 7-dehydrocholesterol but not by cholesterol. Nvd proteins, the authors conclude, might be essential regulators of steroid synthesis and, consequently, of development both in insects and other animal phyla.



Crystallin clear vision

Cataracts – cloudy lenses – are the leading cause of human blindness. How cataracts form is poorly understood although defects in crystallins, the major soluble proteins in lens fibre cells, have been implicated. Now on p. 2585, Goishi and colleagues propose that the defective expression of the protein chaperone αA-crystallin causes the structural protein γ-crystallin to become insoluble and blocks the terminal differentiation of lens fibre cells. Together, these changes cause cataracts. The researchers began their study when they noticed that zebrafish *cloche* mutants, which lack blood cells and blood vessels, also have cataracts. A proteomics analysis indicated that γ-crystallin is insoluble in the cataracts of *cloche* mutants, which led the researchers to discover that αA-crystallin is missing from *cloche* lenses during their development. The overexpression of exogenous αA-crystallin rescued the *cloche* lens phenotype – one of the first times that cataract formation has been blocked in vivo. Thus, as well as providing insights into cataract formation, zebrafish *cloche* mutants could be used to screen for anti-cataract drugs.

Jane Bradbury